UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,831	01/25/2006	Junya Toguchida	Q92863	6132

65565 7590 03/31/2011

SUGHRUE-265550
2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER	
FRAZIER, BARBARA S	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
03/31/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SUGHRUE265550@SUGHRUE.COM
USPTO@SUGHRUE.COM
PPROCESSING@SUGHRUE.COM

Office Action Summary	Application No.	Applicant(s)	
	10/565,831	TOGUCHIDA, JUNYA	
	Examiner	Art Unit	
	BARBARA FRAZIER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/17/10 has been entered.

Status of Claims

2. Claims 35-42 are pending in this application.

3. Cancellation of claims 11 and 20-34 is acknowledged; claims 1-20 and 12-19 already stand canceled.

4. Addition of new claims 37-42 is acknowledged.

5. Claims 35-42 are examined.

Claim Objections

6. **Claims 41 and 42 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only.** Each of claims 41 and 42 recite "The method of claim 40", but also recite "the composition of claim 38", and do not refer to these claims in the alternative.

See MPEP § 608.01(n). Since the claims appear to be drawn to methods, the claims shall be construed as depending from claim 40, and will be examined. However, appropriate correction is required to overcome this objection.

Claim Rejections - 35 USC § 112

7. The rejection of claims 11 and 20-26 under 35 U.S.C. 112, first paragraph is withdrawn in view of Applicant's cancellation of claims 11 and 20-26.

The following rejections are newly applied:

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 37-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37-39 each recite the limitation, "wherein all symbols have the same meanings as those described in Claim 35". However, each of claims 37-39 are written as independent claims. Therefore, it is not clear if the claims intend to further limit, or depend from, claim 35, or if the claims intend to stand on their own as independent claims. As such, the metes and bounds of the claims are unclear. It is suggested that the recitation be removed, and the meanings of the symbols be recited in each of claims 37-39.

Claims 40-42, which depend directly or ultimately from claim 38, do not remedy this deficiency, and therefore are also rejected under 35 U.S.C. 112, second paragraph for reasons stated above.

10. Claims 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 40-42 cites the limitation "the composition of claim 38", but claim 38 is drawn to a method, not a composition. As such, Claims 40-42 fail to have proper antecedent basis from parent claim 38. The Examiner suggests deleting the phrase "the composition of claim 38" and substituting the phrase "the composition" or "said composition" so that the claims properly depend (directly or ultimately) from claim 38.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The rejection of claims 11 and 20-25 under 35 U.S.C. 103(a) as being unpatentable over Cameron et al (WO 98/27976), alone or further in view of Anastassiades (US Patent 6,133,230) is withdrawn in view of Applicant's cancellation of claims 11 and 20-25.

13. The rejection of claim 26 under 35 U.S.C. 103(a) as being unpatentable over Cameron et al (WO 98/27976) alone or further in view of Anastassiades (US Patent 6,133,230) as applied to claims 11 and 20-25, and optionally further in view of Fortier et al (J. Bone Joint Surg., Vol. 84-B, pp. 276-288, 2002) is withdrawn in view of Applicant's cancellation of claim 26.

14. The rejection of claims 27, 28, 35, and 36 under 35 U.S.C. 103(a) as being unpatentable over Cameron et al (WO 98/27976) alone or further in view of Anastassiades (US Patent 6,133,230) as applied to claims 11 and 20-25, and further in view of Tani et al (US Patent 6,110,969) has been modified as follows:

15. Claims 35-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cameron et al (WO 98/27976, previously cited) in view of Tani et al (US Patent 6,110,969, previously cited), and optionally further in view of Anastassiades (US Patent 6,133,230, previously cited) and/or Constan (WO 2004/078169).

The claimed invention is drawn to a method for treating cartilage-related disease, which consists of administering a composition consisting of a substance, as an active ingredient, having an EP2 agonist activity selected from a compound of formula (1-1) as recited in claim 35 (see claim 35). Applicants have elected (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid as the elected species (see claim 36).

Cameron et al teach methods for treating a mammal having a condition which present with low bone mass or other skeletal disorders comprising administering to a

mammal a therapeutically effective amount of an EP2 receptor subtype agonist (abstract). The conditions to be treated include osteoporosis, bone fractures, osteotomy, vertebral synostosis (page 3, lines 20-26). Conditions such as osteoporosis, repair and healing of bone fractures, and bone deformation are cartilage-related diseases, as evidenced by Applicant's specification (page 7, lines 4-23). Additionally, Cameron teaches that the compound used may be applied to the cartilage growth plate (page 79, lines 5-6), and therefore one skilled in the art would reasonably expect that the subject would be in need of stimulating chondrocyte growth in order to form and/or support new bone tissue. The compounds are generally administered in the form of a pharmaceutical composition comprising at least one of the compounds of the invention together with a pharmaceutically acceptable vehicle or diluent (page 80, lines 1-5).

Cameron does not specifically teach that the substance having EP2 agonist activity is (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid, and does not specifically teach that the disease to be treated is one of the diseases listed in claim 35 as amended.

Tani et al teach cycloalkyl-prostaglandin E2 derivatives which can strongly bind on EP2 subtype receptor, and therefore are useful for prevention and/or treatment of abnormal bone formation (abstract). Tani et al exemplify the compound (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid (see Example 17(1), column 94).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to have selected (5Z, 9β, 11α, 13E)-17,17-propano-11,16-

dihydroxy-9-chloroprosta-5,13,19-trienoic acid as the substance having EP2 receptor activity in the methods of the invention of the combined references; thus arriving at the claimed invention. One would be motivated to do so because said species is already known to strongly bind to EP2 receptor, and therefore one skilled in the art would reasonably expect said species to be suitable for the method of Cameron et al, absent evidence to the contrary. One would reasonably expect success from the use of the species of Tani et al with the method of Cameron et al because both references are drawn to treatment of abnormal bone formation using a substance having EP2 agonist activity.

While Cameron et al do not specifically recite that the subject to be treated is "in need of stimulating chondrocyte growth", it is noted that conditions such as osteoporosis, repair and healing of bone fractures, and bone deformation are cartilage-related diseases, as evidenced by Applicant's specification (page 7, lines 4-23). Cameron also teaches that the mammal to be treated may present with low bone mass or other skeletal disorders (abstract) and that the compound used may be applied to the cartilage growth plate (page 79, lines 5-6). Therefore one skilled in the art would reasonably expect that the subject would be in need of stimulating chondrocyte growth in order to form and/or support new bone tissue.

Additionally or alternatively, Anastassiades teaches that exogenous prostaglandin E (a compound functionally related to an EP2 receptor agonist, since both compounds act at prostaglandin receptors) may suppress the cartilage damage and degeneration caused by IL-1 (see col. 1, line 65 - col. 2, line 3). Thus, since exogenous

prostaglandin would be expected to function in a similar manner to a prostaglandin E receptor agonist, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to administer a substance having EP2 agonist activity to a subject in need of stimulating chondrocyte growth, since an EP2 agonist would be expected to perform similarly to exogenous prostaglandin E in suppressing cartilage damage and degeneration, thus allowing for chondrocyte growth.

Additionally or alternatively, Constan et al. teach methods of medical treatment, including facilitating joint fusion, reducing the occurrence of secondary fracture, and facilitating bone healing after limb transplantation, as well as facilitating cartilage repair, using an EP2 selective receptor agonist (abstract). Therefore, since EP2 selective receptor agonists are known to be useful for healing both bone and cartilage, as taught by Constan, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to administer a substance having EP2 agonist activity to a subject in need of stimulating chondrocyte growth, in order to support bone healing as well as facilitate cartilage repair.

Regarding the specific diseases listed in claim 35, it is noted that the claim is drawn to the method steps of administering a composition (an active ingredient consisting of a compound selected from formula (1-1) or a salt thereof) to a population (a subject in need of stimulating chondrocyte growth). Since the method of the combined references is drawn to administering the same composition to the same population, for reasons stated above, the same effects would necessarily take place, including treating the diseases listed in claim 35.

Regarding the methods recited in claims 37-42, it is noted that all of the claims are drawn to the same method steps of administering the same composition (an active ingredient consisting of a compound selected from formula (1-1) or a salt thereof) to the same population (a subject in need of stimulating chondrocyte growth). Since the method of the combined references is drawn to administering the same composition to the same population, for reasons stated above, the same effects would necessarily take place, including those methods recited in claims 37-42.

Response to Arguments

16. Applicant's arguments filed 3/17/10 have been fully considered but they are not persuasive.

Applicants argue that the references of Cameron and Tani relate to bone diseases, rather than cartilage diseases, and Anastassiades does not describe EP2 agonist. Applicants also argue that Cameron teaches away from the claimed invention by teaching bone mass; Applicants assert that cartilage diseases become worse or more serious when cartilage is ossified (pages 14-17 of Remarks filed 3/17/10).

This argument is not persuasive. It is first noted that one of the "cartilage-**related** diseases" to be treated in claim 35 includes injury by sport, which reasonably reads on "bone fractures", as taught by Cameron (page 3, line 21). Additionally, since cartilage provides support to bone, one skilled in the art would still reasonably expect a subject wherein new bone growth is desired (as in Cameron) to also be in need of stimulating chondrocyte growth, in order to support new bone growth. Applicant's arguments that

cartilage diseases become worse or more serious when cartilage is ossified are not persuasive for supporting the assertion that Cameron teaches away from the claimed invention by teaching bone mass, since the references relied upon by Applicants are directed to abnormal conditions, such as cartilage disorders which result in calcification of cartilage, and are not directed to medical treatment which results in an increase in bone mass through use of an active ingredient (in this case, an EP2-selective receptor agonist), as taught in Cameron. While it is noted that Cameron does not specifically describe cartilage formation, it is also noted that, when the references of Cameron, Tani, Anastassiades, and Constan are considered together, the same composition is applied to the same population as that of the claimed invention, for reasons stated above; therefore, the same effects (e.g., treatment of cartilage-related disease or disorder) would necessarily be realized, and therefore the limitations of the claims are met.

In response to Applicant's argument that one skilled in the art would not be able to reasonably predict the recited function (stimulating chondrogenesis) at the administration locus (the cartilage growth plate) (page 17 of Remarks), this argument is not persuasive because EP2-selective receptor agonists are known to facilitate bone repair as well as cartilage repair, as taught by Constan and explained above.

In response to Applicant's arguments regarding the Anastassiades reference (page 18 of Remarks), it is noted that motivation to combine the references is provided within the rejection; since exogenous prostaglandin would be expected to function in a similar manner to a prostaglandin E receptor agonist, it would have been obvious to a

person having ordinary skill in the art at the time the invention was made to administer a substance having EP2 agonist activity to a subject in need of stimulating chondrocyte growth, since an EP2 agonist would be expected to perform similarly to exogenous prostaglandin E in suppressing cartilage damage and degeneration, thus allowing for chondrocyte growth (also see rejection, above).

In response to Applicant's arguments regarding the Tani reference (page 18 of Remarks), it is noted that abnormal bone formation, taught by Tani, includes cartilage disorders, as evidenced by Applicant's remarks (e.g., see page 16 of Applicant's Remarks filed 3/17/10), and therefore the subjects treated by Tani would be in need of simulating chondrocyte growth. Additionally, conditions such as bone deformation are cartilage-related diseases, as evidenced by Applicant's specification (page 7, lines 4-23), and therefore the subjects treated by Tani would be in need of simulating chondrocyte growth. While Applicants assert that the diseases recited in amended claims 35 and 36 cannot be treated by increasing bone mass, it is noted that the method of the combined references is drawn to administering the same composition to the same population as that of the claimed invention; therefore, the same effects would necessarily take place, including treating the diseases listed in claim 35.

Therefore, it is the Examiner's position that the claims are rendered obvious.

The following rejection is newly applied:

17. Claims 35-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Constan et al (WO 2004/078169) in view of Tani et al. (Bioorg. Med. Chem., 10(4), pp. 1107-1114, 2002).

The claimed invention is drawn to a method for treating cartilage-related disease, which consists of administering a composition consisting of a substance, as an active ingredient, having an EP2 agonist activity selected from a compound of formula (1-1) as recited in claim 35 (see claim 35). Applicants have elected (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid as the elected species (see claim 36).

Constan et al. teach methods of medical treatment, including facilitating cartilage repair, using an EP2 selective receptor agonist (abstract). Constan teaches that EP2 selective receptor agonists that can be used in its invention include those by Tani et al. in *Bioorganic & Medicinal Chemistry* (2002), pp. 1107-1114 (see page 23, lines 11-15), which teaches compounds used in the methods of the claimed invention (see description, below). The compounds are generally administered in the form of a pharmaceutical composition comprising at least one of the compounds of the invention together with a pharmaceutically acceptable vehicle or diluent (page 50, lines 14-16), in amounts effective to treat the disease/condition of the subject being treated (page 51, lines 17-21). Since the compound may be given for the purpose of facilitating cartilage repair, the subject to whom the compound is administered would be in need of stimulating chondrocyte growth.

Constan does not exemplify the use of the EP2-receptor agonists of Tani sufficiently to anticipate the claims; therefore, the rejection is made under obviousness.

Tani et al. teach 9-beta-chloro PG analogues which were found to be potent and selective EP2-receptor agonists (abstract). Compounds having highest selectivity (and lowest ED50) were compounds 4a and 4c, which correspond to the compounds of instant claim 36 (see page 1109, Scheme 3, and page 1110, Table 2).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to select the compounds of Tani et al. as the EP2-receptor agonists in the invention of Constan; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the compounds of Tani (which correspond to the compounds of instant claim 36) provide the advantage of high selectivity for the EP2-receptor, as taught by Tani, and therefore would be expected to have the most favorable activity. One would reasonably expect success from the use of the compounds of Tani in the invention of Constan because Constan teaches the compounds of Tani are suitable EP2-receptor agonists in its invention.

Regarding the specific diseases listed in claim 35, it is noted that Constan teaches the use of EP2-selective receptor agonists for facilitating cartilage repair (abstract), and that claim 35 is drawn to the method steps of administering a composition (an active ingredient consisting of a compound selected from formula (1-1) or a salt thereof) to a population (a subject in need of stimulating chondrocyte growth). Since the method of the combined references is drawn to administering the same

composition to the same population, for reasons stated above, the same effects would necessarily take place, including treating the diseases listed in claim 35.

Regarding the methods recited in claims 37-42, it is noted that all of the claims are drawn to the same method steps of administering the same composition (an active ingredient consisting of a compound selected from formula (1-1) or a salt thereof) to the same population (a subject in need of stimulating chondrocyte growth). Since the method of the combined references is drawn to administering the same composition to the same population, for reasons stated above, the same effects would necessarily take place, including those methods recited in claims 37-42.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Ashwin Mehta/
Primary Examiner, Art Unit 1638